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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/190,246	11/13/98	PARRINGTON M	1038-865MIS

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EXAMINER	
WILSON,M	
ART UNIT	**PAPER NUMBER**
1633	17

DATE MAILED: 05/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	09/190,246	PARRINGTON ET AL.	
	Examiner	Art Unit	
	Michael Wilson	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-19 and 36-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-19 and 36-38* is/are rejected.

7)☒ Claim(s) *11* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Applicant's arguments filed 1-8-01, paper number 15, have been fully considered but they are not persuasive. The amendments filed 1-8-01 and 1-25-01, papers 15 and 16 have been entered. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claims 2-5 and 20-35 have been deleted. Please make sure to request the cancellation of claims clearly at the beginning of the amendment. Claims 1, 6-19 and 36-38 are pending and under consideration in the instant application.

Specification

1. The attempt to incorporate subject matter into this application by reference to US application 08/923558 is improper because the method of immunizing the mice is considered essential to practice the invention. The relevant information regarding the method of immunizing the control group should be included in the instant specification. The results obtained in applications 08/923,558, 08/476,397 and 08/896,500 are not included in the instant specification (page 26, line 22). The comparison of the results obtained in example 3 of the instant invention to the results obtained in another application is essential subject matter; therefore, such results should be included in the specification.

2. The blanks for US Patent applications (page 23, line 25; page 24, line 23) have been filled in with "US Patent application number 09/190245 filed November 13, 1998". However, the status of 09/190245 must be updated to indicate that 09/190245 has been abandoned.

3. The addition of the ATCC designation 203461 deposited 11-18-98 on page 22, line 10 is new matter. The filing date of the instant application is 11-13-98. Since the deposit was made 5 days after the application was filed, it is not evident that the deposit was in applicants possession at the time of filing. Furthermore, applicants have not provided any evidence that the inventors of the instant application deposited 203461 or that the deposit will be maintained according to the Budapest treaty. Requirements for deposits are provided below.

If the deposit was made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when a deposit is made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and address of the depository is required. Furthermore, unless deposit was made at or before the time of filing, a declaration filed under 37 C.F.R. 1.132 is necessary to construct a chain of custody. The declaration, executed by a person in a position to know, should identify the deposited material by its depository accession number, establish that the deposited material is the same as that described in the specification, and establish that the deposited material was in applicant's possession at the time of filing. In re Lundak, 27 USPQ 90.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that,

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years of 5 years after the last request or for the enforceable life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of the deposit was made and that the test results indicated that said biological material was viable (see 37 CFR 1.807); and,

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

As required under 37 C.F.R. § 1.809(d), the specification shall contain: (1) the accession number for the deposit; (2) the date of deposit; (3) a description of the deposited biological material sufficient to identify it and to permit its examination; and (4) the name and address of the depository.

Claim Objections

4. Claim 11 is objected to because of the following informalities: the word "to" should be inserted after the word adjacent on line 2. Appropriate correction is required. Applicants argue claim 11 has been canceled, but claim 11 has not been canceled.

Claim Rejections - 35 USC § 112

5. Claims 1, 6-19 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 as newly amended recites the limitation of a protein fragment that induces production of antibodies that specifically react with the RSV protein. The specification does not provide written description for any fragments of the F or G proteins of RSV that induce production of antibodies as claimed. Nor were such fragments known in the art at the time of

filing as there was a lack of teaching regarding fragments of F or G proteins of RSV that induced antibodies. Without such guidance, it would have required one of skill in the art at the time the invention was made undue experimentation to determine any fragment of the F or G proteins of RSV that induced antibodies as claimed.

6. Claims 1, 6-19 and 36-38 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions, does not reasonably provide enablement for enhancing the immunoprotective ability of the paramyxovirus protein when expressed *in vivo* from the vector in a host. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for reasons of record.

Claims 1 and 11 recite the limitation of "enhancing the immunoprotective ability of the paramyxovirus protein when expressed *in vivo* from the vector in a host." Claim 36 recites the limitation of an "immunoeffective amount" of a vector of claim 1. The specification details the production of antibodies specific for RSV proteins after immunization of mice with the claimed construct. At no point is the specific antibody response of the mice shown to be protective. The specification states 1 out of 6 mice receiving pMP44 were infected with RSV upon challenge (page 26, line 18) and that only 83% protection was obtained indicating that some infection of the lungs occurred. The protective immune response is the hallmark of a vaccine. The specification does not provide adequate guidance for one of skill to enhancing the immunoprotective ability of the paramyxovirus protein when expressed *in vivo* from the vector in a host. The specification

does not enable an immunoeffective amount of a vector as broadly claimed or obtaining immunoprotection.

Claim 1 as newly amended recites the limitation of a protein fragment that induces production of antibodies that specifically react with the RSV protein. The specification does not teach any fragments of the F or G proteins of RSV that induce production of antibodies. Nor were such fragments known in the art at the time of filing as there was a lack of teaching regarding fragments of F or G proteins of RSV that induced antibodies. Without such guidance, it would have required one of skill in the art at the time the invention was made undue experimentation to determine any fragment of the F or G proteins of RSV that induced antibodies as claimed.

7. Claims 1, 6-19 and 36-38 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the phrase "the first, second and third DNA sequence being under transcriptional control of a promoter" is unclear. It is unclear whether the first, second and third DNA sequences are all operatively linked to one promoter or if they are each operatively linked to their own promoter. Clarification is required.

Claim 1 is indefinite because it is unclear whether the phrase "and that enhances the immunoprotective ability of the RSV protein or fragment thereof" on line 11 refers to the third DNA sequence or the first DNA sequence. The phrase is also grammatically incorrect as it relates

to "a third DNA sequence operatively linked to the first DNA sequence" because of the words "and that". Clarification is required.

Claim 1 is indefinite because the structure of the third DNA sequence is unclear. As written, it is unclear where the third sequence is in relation to the first and second sequence. Since the vector may not be introduced into a host, the function of the third sequence may not determined. It is unclear how the third sequence in claim 11, the third sequence that are splice sites (claim 12) or the rabbit β-globin intron II correlate to the third sequence in claim 1. Therefore, the metes and bounds of the structure of the third sequence cannot be determined.

The term "adjacent" in claim 11 remains indefinite. It is unclear whether the term is intended to mean the 3rd sequence is directly adjacent to the 2nd sequence or is operatively linked in a nearby location in relation to the 2nd sequence.

The phrase "to enhance the immunoprotective ability of a paramyxovirus protein" (claims 1 and 11) is indefinite because the it is unclear which proteins have immunoprotective ability and which sequence enhance such ability. While some paramyxovirus proteins may induce an immune response that provides protection against viral challenge, it is not clear how such an effect correlates to immunoprotective ability of a paramyxovirus protein. Since it is unclear what applicants consider the immunoprotective ability of a protein, it cannot be determined when such an ability has been enhanced.

The phrase "when expressed *in vivo* from the vector in a host" (claim 11) is unclear. It is unclear whether "from the vector" refers to the protein or the expression. It is unclear whether

"in a host" refers to the presence of a vector in a host, a protein in a host or expression that occurs in a host.

Claim 11 is indefinite because it is unclear how the 3rd DNA sequence in claim 11 correlates to the 3rd DNA sequence in claim 1. It does not appear that claim 11 further limits claim 1.

The phrase "aberrant mRNA splicing *in vivo*" (claim 12) is indefinite because it is unclear whether applicants intend to distinguish aberrant mRNA splicing *in vivo* from mRNA splicing *in vitro* or whether applicants are merely indicating that aberrant mRNA splicing does not occur when the vector is used *in vivo*.

It is unclear how the location of the third nucleotide sequence as described in claim 13 correlates to the first, second or third sequence described in claim 12 or claim 1 because of the confusion regarding the third sequence in claims 1 and 12 as newly written.

The phrase "immunoeffective amount" in claim 36 is indefinite because the specification does not define what applicants consider such an amount and such an amount cannot be determined in the art. Therefore, the metes and bounds of what applicants consider "immunoeffective amount" cannot be determined.

Claim Rejections - 35 USC § 102

8. Claims 1, 6-16, 18, 36 and 37 remain rejected under 35 U.S.C. 102(e) as being anticipated by Parrington (Parrington, US Patent 6,060,308, May 9, 2000) for reasons of record.

Parrington teach a Semliki forest viral vector expressing the F or G proteins of RSV. The sequence contains the CMV immediate early promoter and rabbit β-globin intron II (column 4, line 11). The limitation of a third sequence operatively linked to the first DNA sequence (claim 1) is equivalent to the DNA encoding the RSV proteins because the phrase "that enhances the immunoprotective ability..." is indefinite (see 112/2nd above) and is an intended use which does not have to occur. As such the phrase "that enhances the immunoprotective ability..." is not given patentable weight in considering art.

The limitation of the third DNA sequence located adjacent to the first sequence and between the first sequence and the promoter (claim 11) and a third DNA sequence that comprises a pair of splice sites (claim 12) is equivalent to the DNA sequence adjacent to the alphavirus sequence and the DNA sequence between the alphavirus sequence and the promoter taught by Parrington. Such a sequence comprises a "pair of splice sites" (claim 12) because the sequence can be spliced at any two sites. In addition, the phrases "to enhance the immunoprotective ability..." (claim 11) and "that prevent[s] aberrant mRNA splicing *in vivo*" (claim 12) are intended uses and do not bear patentable weight when considering art rejections. Thus, Parrington anticipates the claims.

Applicants argue that Parrington does not teach a vector encoding the CMVIE promoter or rabbit β-globin intron II. Applicants argument is not persuasive because Parrington states these elements are incorporated into the alphaviral vectors encoding the F or G proteins of RSV.

Claim Rejections - 35 USC § 103

9. Claims 1, 6-16, 18, 36 and 37 remain rejected under 35 U.S.C. 103 as being anticipated by Dubensky (Dubensky et al., US Patent 5,814,482, Sept. 29, 1998) in view of Li (Li et al., WO 96/40945, Dec. 19, 1996) for reasons of record.

Dubensky teach an alphaviral vector encoding RSV proteins (claim 10 of '482). The alphaviral vector sequence is the "first DNA sequence" and the DNA encoding the RSV protein is the "second DNA sequence" and third DNA sequence" as claimed. The alphavirus of Dubensky is Semliki forest virus (column 11, line 67) which is equivalent to the sequence contained in plasmid pSFVI (claim 9).

The limitation of a third sequence operatively linked to the first DNA sequence (claim 1) is equivalent to the DNA encoding the RSV proteins because the phrase "that enhances the immunoprotective ability..." is indefinite (see 112/2nd above) and is an intended use which does not have to occur. As such the phrase "that enhances the immunoprotective ability..." is not given patentable weight in considering art.

The limitation of the third DNA sequence located adjacent to the first sequence and between the first sequence and the promoter (claim 11) and a third DNA sequence that comprises a pair of splice sites (claim 12) is equivalent to the DNA sequence adjacent to the alphavirus sequence and the DNA sequence between the alphavirus sequence and the promoter taught by t Dubensky. Such a sequence comprises a "pair of splice sites" (claim 12) because the sequence can be spliced at any two sites. In addition, the phrases "to enhance the immunoprotective

ability..." (claim 11) and "that prevent[s] aberrant mRNA splicing *in vivo*" (claim 12) are intended uses and do not bear patentable weight when considering art rejections.

Dubensky does not teach the nucleic acid sequence of the RSV F or G proteins.

However, at the time of filing, Li taught a vector encoding the RSV F and G proteins under the control of the CMV immediate early promoter and comprising the rabbit β-globin intron II (page 14, lines 5-21).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the expression vector encoding RSV proteins taught by Dubensky to deliver the F or G protein taught by Li. Motivation is provided by Li by stating the F or G protein induce an immune response in a host (page 15, line 17). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an alphaviral vector encoding an RSV protein as taught by Dubensky wherein the F or G protein of RSV are used with the rabbit β-globin intron II sequence between the alphavirus sequence and the CMVIE promoter as suggested by Li (page 14, line 10). It would have been obvious to one of ordinary skill in the art at the time the invention was made to place the HDV ribozyme on the 3' end of the alphavirus sequence to insure deletion of the polyA termination sequence as suggested by Dubensky (column 71, line 17) who also place the HDV ribozyme on the 3' end of the alphavirus sequence.

Applicants argue that the phrases "to enhance", "that prevent" or "that enhances" bear patentable weight because they describe the function of the DNA sequence. Applicants argument is not persuasive. The mere description of a DNA sequence as a sequence "that enhances the

immunoprotective ability of the RSV protein" does not describe the structure of the sequence. The description of the sequence does not adequate describe the function of the sequence because the protein may not be immunoprotective and the vector may not be introduced into a host. As such the descriptions used do not adequately describe the structure or function of the sequence. Terms such as "promoter," "regulatory element" and "enhancer" which were known in the art to describe the functions of DNA sequences are adequate to describe the function of sequences that are promoters, regulatory elements or enhancers. The phrases "that enhances...", "that prevents" or "to enhance" as claimed do not adequately describe the structure or function of the DNA sequences.

Applicants argue Li does not teach using the Semliki virus. Applicants argument is not persuasive because claims 1, 6, 7, 10-19 and 36-38 are not limited to the Semliki virus and because the combined teachings of Dubensky and Li provide adequate guidance to use the Semliki virus.

Double Patenting

10. Claims 1, 6-16, 18, 36 and 37 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5, 6, 8 and 18-21 of U.S. Patent No. 6,060,308. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass vectors lacking a Sei restriction site and the pMP37 vector claimed in 6,060,308. The pMP37 vector is disclosed in the

instant application on page 22, line 10 and in Fig. 1B, top left which according to U.S. Patent 6,060,308 lacks a SpeI restriction site (claims 1 and 8). Therefore, any of the vectors claimed in the instant invention could be linearized by SpeI restriction and lack a Spe I restriction site which is taught on page 24, line 24 as are the vectors claimed in '308. Therefore, the vectors of claims 1-3, 5, 6, 8 and 18-21 of US Patent 6,060,308 are vectors as claimed in the instant invention.

Applicants argue the claims are patentably distinct for reasons cited above regarding the 102 using Parrington (US Patent 6,060,308). Applicants arguments are not persuasive for reasons cited above in the discussion of Parrington under 102.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-2982.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

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